AD

DRUG REGULATORY AFFAIRS

ANNUAL REPORT

ARTHUR M. HOROWITZ

JULY 15, 1988

Supported by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701-5009

Contract No. DAMD17-86-C-6189

Engineering and Economics Research Inc.
20251 Century Boulevard
Germantown, Maryland 20874

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19 ABSTRACT (Continue on reverse if necessary and identify by block number)

The timely and efficient execution of the U.S. Army Medical Materiel Pharmaceutical Development Program requires a thorough knowledge of regulations issued by the U.S. Food and Drug Administration. In order to accomplish the execution of this drug development program, the Pharmaceutical System Project Management Office, an element of the U.S. Army Medical Materiel Development Activity (USAMMDA), awarded a multi-year contract to Engineering and Economics Research (EER) and its subcontractor, Oxford Research International Corporation (ORIC). The EER/ORIC team has provided the necessary managerial and technical expertise to complete the preparation and assembly of IND/NDAs. A total of 5 tasks were submitted to the contractor during the second contract year. All task orders were completed or are in progress within the projected delivery schedule and cost estimate.

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FOREWORD

For the protection of human subjects the investigator(s) have adhered to policies of applicable Federal Law 45CFR46.

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1.0 Introduction

The Pharmaceutical Systems Project Management Office (PSPMO), an element of the U.S. Army Medical Materiel Development Activity (USAMMDA) holds the responsibility for planning, organizing, directing and controlling all aspects of drug development. Every stage of drug development must be in compliance with current FDA requirements. The principal objective of this contract is to prepare and assemble drug-specific, FDA-related documentation as well as a data management system to track the status of regulatory documentation. The contractor has furnished the necessary personnel, facilities, equipment and supplies to complete the scope of work as prescribed in each task order. In accordance with Section F of the Drug Regulatory Affairs contract, quarterly reports describing the technical progress and financial status for each Task Order have been submitted. This second Annual Report describes the work performed by the contractor for the 12 month period of July 1, 1987 to June 30, 1988.

2.0 Discussion

2.1 Task 86-01 Project Planning, Coordination and Integration

Task 86-01 requires the development and maintenance of a planning, coordinating and task integration infrastructure for the Drug Regulatory Affairs Contract. This infrastructure provides for overall project planning and tracking, individual task planning, monthly project review meetings, quarterly progress reports and attendance at relevant professional meetings and symposia. A recent modification to this task requests the preparation of monthly progress reports.

2.1.1 Overall Project Planning and Tracking

A cost and schedule tracking system has been developed by EER to assist in the preparation of monthly, quarterly and annual reports. An inventory control system to account for property purchased under the subject contract, but for which the government retains property, has been implemented.

A central filing system has been established for all DRA-related documents. The file is maintained in the DRA library.

2.1.2 Individual Task Planning

Five new task orders were received from USAMMDA during this contract term. Two modifications to the existing task orders were approved. The individual task orders and dates when these tasks were approved by the contracting officer are summarized as follows:

Task Order	Date Task Order Approved
Task 86-02, Modification 3	March 4, 1988
Task 86-02, Modification 4	March 24, 1988
Task 87-06	September 21, 1987
Task 87-07	October 7, 1987
Task 87-08	October 23, 1987
Task 87-09	January 22, 1988
Task 88-12	April 28, 1988

The following modifications to existing task orders were sent to USAMMDA for approval:

Task Order	Date TEP Submitted
Task 86-02, Modification 5	June 29, 1988
Task 86-03, Modification 2	June 29, 1988
Task 86-04, Modification 1	June 29, 1988

2.2 Task 86-02 Preparation of Annual IND Progress Reports

This task requires the preparation of annual progress reports on outstanding IND Submissions. Fifteen INDs require the preparation of an annual report. Assessment reports were prepared prior the preparation of the annual report to identify outstanding documentation necessary for the completion of the report.

Upon receipt of requested documentation from USAMMDA, the contractor prepared the Annual Report. Anniversary dates for FDA receipt of new annual reports and date last annual report was prepared are described in the following table:

IND No.	Product	Category	Anniversary Date	Date of Last Submission
5,509	Phosphorothioic (WR 2,721)	Antiradiation	18 Feb 1969	04 Dec 1986
8,990	Mefloquine (WR 142,490)	Antimalarial	23 Jun 1972	03 Jul 1986
9,847	Halofantrine (WR 171,669)	Antimalarial	06 Jun 1973	11 Dec 1986
12,735	Enpiroline (WR 180,409)	Antimalarial	23 Aug 1976	03 Jul 1986
14,150	Pentostam (WR 229,870)	Antileishmanial	01 Feb 1978	10 Apr 1987
14,252	Temefos	Pediculicide	10 Mar 1978	16 Jun 1988
16,666	Ribavirin	Antiviral	27 Jul 1979	22 Jun 1987
17,326	Phosphorothioate (WR 638)	Antishock	29 Jun 1967	14 Mar 1984
21,084	WR 6,026	Antileishmanial	03 Nov 1982	29 Dec 1987
23,509	Pyridostigmine (WR 270,710)	Antidote	30 Jan 1984	15 Jun 1987
26,740	Ketoconazole	Antileishmanial	11 Jul 1985	03 Aug 1987
27,503	Atropine sulfate	Antidote	20 Nov 1985	27 May 1987
28,301	Atropine+2PAM	Antidote	29 Apr 1986	27 May 1987
30,726	Ketoconazole vs pentostam	Antileishmanial	29 Sep 1987	----New----
30,899	Pyridostigmine sust'd release	Antidote	07 Dec 1987	----New----

2.2.1 Task 86-02, Modification #1

This Task Order requires an evaluation of all existing data, information and other pertinent material relating to oral pyridostigmine (IND 23,509).

2.2.2 Task 86-02, Modification #2

This Task Order, consisting of ten subtasks, requires the collection and evaluation of data and preparation of annual IND progress reports.

2.2.2.1 Ketoconazole.

This subtask requires the preparation of an assessment report and an annual IND progress report for ketoconazole (IND 26,740; WR 248,310). Annual report submitted to USAMMDA on August 3, 1987.

2.2.2.2 Phosphorothioic Acid.

This subtask requires the duplication and filing of Supplement #9 in the DRA library (IND 5,509; WR 2,721).

2.2.2.3 Mefloquine.

This subtask requires the analysis of four clinical studies comprised of 506 patients; preparation of four clinical summary reports; and submitting these reports to the FDA as Clinical Information Reports (IND 8,990; WR 142,490).

Clinical Studies

- Study No. 1 (Comparative treatment of 162 patients treated with Enpiroline or Mefloquine
- Study No. 2 (Mefloquine pharmacokinetic study of 39 patients)

- o Study No. 3 (Comparative treatment of 80 patients treated with mefloquine, quinine and tetracycline or quinine and doxycycline)
- o Study No. 4 (Comparative treatment of 225 patients treated with quinine or mefloquine)

2.2.2.4 Halofantrine.

Upon receipt of the bioavailability report from WRAIR, this subtask requires the preparation of the annual IND progress report for IND 9,847; WR 171,669.

2.2.2.5 Enpiroline.

This subtask requires the preparation of an annual IND progress report for IND 12,735; WR 180,409. Clinical data from a study comprised of 162 patients treated with mefloquine or enpiroline will be used in the preparation of this report.

2.2.2.6 WR 6,026.

This subtask requires the analysis of a pharmacokinetic study and preparation of an annual IND progress report (IND 21,084).

2.2.2.7 Pentostam.

This subtask requires the collection, duplication and analysis of clinical data from 43 patients as well as preparation of an annual IND progress report (IND 14,150; WR 229,870).

2.2.2.8 Temefos.

This subtask requires the preparation of an annual IND progress report for IND 14,252.

2.2.2.9 Atropine Sulfate, USP.

This subtask requires the preparation of an annual IND progress report (IND 27,503).

2.2.2.10 Atropine 2-PAM.

This subtask requires the preparation of an annual IND progress report (IND 28,301).

2.3 Task 86-03 Preparation of an NDA for Ribavirin

This task requires the collection and analysis of preclinical and clinical information for the parenteral formulation of ribavirin, as well as the preparation and submission of an NDA in the format required by 21 CFR 314.50.

2.3.1 Ribavirin NDA Team Meetings

On November 10, 1987 a Ribavirin pre-NDA meeting was held at the FDA to discuss the clinical documents submitted to FDA. Current regulations require a minimum of two independent and well-controlled studies for each clinical indication. The US Army has submitted data for two viral diseases, Lassa and Endemic Hemorrhagic Fever (HFRS). The FDA has commented that there was insufficient data for two distinct clinical indications and requested new studies using a greater study population. The FDA

expressed a willingness to work with Army in designing additional studies, despite the erratic, cyclical nature of the diseases. The use of historical data may be used as the control group in future studies, thus enabling all subjects in the treatment protocol to receive the drug. Possible future actions include revising the current treatment protocol in Korea; initiating new studies in China when the next disease epidemic occurs and considering additional protocols for Lassa Fever.

The FDA requested additional preclinical toxicology data. Dr. Browder (FDA pharmacologist and reviewer) suggested that USAMMDA review the toxicology data submitted in the Viratek aerosol formulation NDA and compare this data to the toxicology data package submitted by USAMMDA (parenteral formulation).

The Command decided to submit the remaining portions of the NDA (Clinical section and labeling) rather than initiating new clinical studies.

A follow-up NDA team meeting was held on May 5, 1988 and attended by representatives of USAMMDA, USAMRIID and the EER/Oxford team. The purpose of this meeting was to identify documentation required to file the NDA. The NDA will be reviewed by a new FDA Division, Antiviral Drugs under the direction of Dr. Ellen Cooper. The projected target date for the completion of the NDA was estimated as 6 - 8 months (December 1988 - February 1989).

2.4 Task 86-04 Data Management for Document Presentation

The regulatory library database management system was revised to include the IND amendment serial number, the drug name, and an indication whether the document was for a final NDA application. Data within the system has been verified twice against the physical documents, with a third review in progress. Six filing cabinets were added to the document room (which is secured by a cypher lock) to store additional DRA material. The lock combination was changed after two employees with access to the number left EER employment. A new 40 megabyte hard disk drive was received to replace the current 20 megabyte drive which is considered unreliable by our service contractor, Astronautics. The CTS external modem was swapped for a Hayes internal modem and Hayes Smartcom II communications software was installed. The text processing software WordPerfect was upgraded from version 4.1 to version 4.2.

A duplicate database management system is maintained at USAMMDA which is updated periodically with information and program updates transferred via DC 1000 20 megabyte magnetic tapes. Problems in using the tape-drive were encountered at EER and many new tapes could not be properly servo-written or formatted. A bulk-tape eraser is now used to clear all information from tapes when initial formatting fails.

Discussions were held with representatives at the FDA who specialize in regulatory document tracking. Their comments together with user feedback at EER were

incorporated into a new database architecture and system design. This design reflects more closely the categories and types of information tracked by the FDA.

2.5 Task 87-01 Halofantrine

The purpose of this task was to determine whether there was adequate data to support an NDA for Halofantrine. This drug is being studied for use in the prophylaxis and treatment of malaria caused by P. falciparum. This report identified both the strengths and weaknesses of the manufacturing and control, pre-clinical and clinical sections of the NDA.

2.6 Task 87-02 Literature Review of Cholinergic Inhibitors

This task requires the preparation of a literature review on the toxicology resulting from inhibition of acetylcholinesterase on the neuromuscular junction. This review was written for inclusion in Section 6 of the IND. An executive summary of the literature was also prepared for review by a Pyridostigmine Blue Ribbon Committee.

2.7 Task 87-03 Pharmacokinetic Analysis of Atropine

The purpose of this task was to prepare a scientific report for the study: "A Comparative Analysis of the Pharmacokinetic Properties of Intramuscularly-Administered Atropine in Humans and Rhesus Monkeys." This was an open-label comparative study in which each subject received a single intramuscular dose of

atropine 0.025 to 0.035 mg/kg for the monkeys and the approximate equivalent dose for humans). The study demonstrated that both species showed relatively similar mean values for peak plasma atropine concentration and for the time after atropine intramuscular administration required to reach this peak. The monkey eliminates atropine from plasma approximately twice as rapidly as man, as evidenced by the lower plasma half-life, the higher mean elimination constant and plasma atropine versus time AUC calculations. The report speculated that administration of a single dose of atropine in man would result in approximately twice the duration of effective atropine prophylactic activity in man for an equivalent mg/kg dose in the monkey.

2.8 Task 87-04 Pyridostigmine Pharmacokinetic Analysis

The requirements of this task include: (1) Summarization of data on cholinesterase inhibition with descriptive statistics for time and dose; (2) Preparation of a pharmacokinetic report on plasma pyridostigmine levels and a correlation analysis of cholinesterase inhibition and associated plasma pyridostigmine levels.

A comparative bioavailability cross-over design study of 18 subjects carried out at a dose level of 30 mg confirmed no significant difference between the tablet and syrup formulation of pyridostigmine.

This open, cross-over clinical study demonstrated that oral administration of pyridostigmine, 0.40 mg/kg to 0.90 mg/kg, produces a proportional increase in RBC acetylcholinesterase inhibition. The 0.40 mg/kg dose

(approximately 30 mg) inhibits RBC acetylcholinesterase in the range of 20 to 40 percent. This degree of acetylcholinesterase inhibition is considered to offer optimal protection against nerve gas poisoning.

2.9 Task 87-03 Pyridostigmine Acetylcholinesterase Statistical Study

This task requires the analysis of a pharmacokinetic study conducted in Rhesus monkeys and man to determine the dose effect relationship of pyridostigmine and inhibition of acetylcholinesterase between the two species. The results from this study will be used to support the hypothesis that extrapolation of monkey data to man is valid.

This open cross-over study was conducted in 12 subjects orally treated with 0.40, 0.57, 0.71 and 0.40 mg/kg pyridostigmine syrup. The study demonstrated a large individual variation in the pharmacokinetic response of pyridostigmine in humans and monkeys.

The pyridostigmine plasma AUC is greater in man as compared to monkey. The AUC response for both species was shown to be dose dependent and linear for dose. However, a non-linear relationship was observed with respect to RBC acetylcholinesterase inhibition and pyridostigmine dose. These results appear to indicate that higher doses of pyridostigmine probably would not result in a linear increase in acetylcholinesterase inhibition.

2.10 Task 87-06 IND Preparation for Pentostam-Ketoconazole

This task requires the preparation of a "Notice of Claimed Investigational Exemption for a New Drug" (IND) in accordance with 21 CFR 312.10 (old format) [assigned IND# 30,726].

2.11 Task 87-07 Technical Support for Army Pharmaceutical Advisory Committee Meeting

This task requires scientific and regulatory review of cumulative IND summaries of five drugs; photocopy and collate specified documents to be presented to the Army Pharmaceutical Advisory Committee (WRAIR).

2.12 Task 87-08 IND Preparation for the Oral Sustained Release Formulation of Pyridostigmine

This task requires the preparation of a "Notice of Claimed Investigational Exemption for a New Drug" (IND) in accordance with 21 CFR 312.10 (old format) [assigned IND# 30,899].

2.13 Task 87-09 Pyridostigmine, Amendment to Clinical Section

This task requires the preparation of an Amendment to the Clinical Section of IND 23,509 by providing analysis of the investigation conducted by Allstatt and subsequent comments by Dr. Edward Purich.

2.14 Task 88-12 IND Preparation for Schistosome Topical Antipenetrant

This task requires the preparation of a "Notice of Claimed Investigational Exemption for a New Drug" and clinical protocol.

3.0 Status of Accomplishments

A total of 5 tasks were submitted to the contractor during this performance period. All tasks/subtasks are proceeding on schedule. The following table summarizes the technical progress for each task/subtask.

SUMMARY TABLE
TASK ORDER TECHNICAL PROGRESS

Task Order	Deliverable	Submission Date	Status of Task Order	Status of Subtask
86-01			in progress	
	1st Quarterly Report	10/15/87		complete
	2nd Quarterly Report	01/15/88		complete
	3rd Quarterly Report	04/15/88		complete
	4th Quarterly Report	07/15/88		complete
	2nd Annual Report	07/15/88		complete
	Monthly Reports	08/01/87 - 07/01/88		complete
86-02			in progress	
	Planning Task	06/18/86		complete
	Planning Task	11/16/86		complete
	Ketoconazole (original)	11/16/86		complete
	Enpiroline (original)	11/16/86		complete
	Pyridostigmine			
	Draft Annual IND Report	06/09/88		complete
	Final Annual IND Report	06/29/88		complete
	Ketoconazole			
	Draft IND Annual Report	06/26/87		complete
	Final IND Annual Report	07/13/87		complete
	Phosphorothioic Acid			
	Mefloquine			
	Collect and summarize clinical data			complete
	Draft Clinical Information			
	Amendment Reports			
	Study No. 1	12/07/87		gov't review
	Study No. 2	02/05/88		gov't review
	Study No. 3	04/28/88		gov't review
	Study No. 4			in-progress
	Draft IND Annual Report	06/29/88		gov't review
	Final IND Annual Report			
	Halofantrine			
	Draft IND Annual Report	06/29/88		gov't review
	Final IND Annual Report			
	Temefos			
	Final IND Annual Report	06/09/88		complete
	Enpiroline			
	Draft IND Annual Report	06/29/88		gov't review

Task Order	Deliverable	Submission Date	Status of Task Order	Status of Subtask
	Final IND Annual Report			
	Antileishmanial (WR 6,026)			
	Draft IND Annual Report	12/17/87		gov't review
	Final IND Annual Report			
	Pentostam			
	Summarize Ballou clinical study	09/18/87		complete
	Draft IND Annual Report	06/29/88		gov't review
	Final IND Annual Report			
	Atropine Sulfate, USP			
	Draft Annual IND Report	06/09/88		gov't review
	Final Annual IND Report			
	Atropine-2PAM			
	Draft Annual IND Report			
	Final Annual IND Report			
86-03	Ribavirin		in progress	
	Original Administration Subtask	11/16/86		complete
	NDA Preparation			
	Mfg. and Control Section	04/01/87		complete
	Pre-Clinical Section	06/08/87		complete
	Clinical Section			in progress
86-04	Document Management			in progress
	Tape Cartridge Delivery	09/29/87		complete
87-01	Halofantrine			
	NDA Evaluation	03/23/87		gov't review
87-02	Acetylcholinesterase Literature Review		complete	
87-03	Atropine Pharmacokinetic Analysis		complete	
87-04	Pyridostigmine Pharmacokinetic Analysis		in progress	
	Draft Clinical Report	03/27/87		gov't review
	Final Clinical Report			
87-05	Pyridostigmine-Acetylcholinesterase Statistical Study		in progress	
	Draft Clinical Report	06/26/87		gov't review
	Final Clinical Report			

Task Order	Deliverable	Submission Date	Status of Task Order	Status of Subtask
87-06	IND Preparation for Pentostam-Ketoconazole		complete	
	Draft IND	10/02/87		complete
	Final IND	10/02/87		complete
87-07	WRAIR Pharmaceutical Advisory Committee Support	10/09/87	complete	complete
87-08	IND Preparation for Sustained Release Pyridostigmine		complete	
	Draft IND	11/20/87		complete
	Final IND	11/20/87		complete
87-09	Pyridostigmine Clinical Report		complete	
	Draft Clinical Amendment Report	03/02/88		complete
	Final Clinical Amendment Report	06/28/88		complete
88-12	IND Preparation for Niclosamide		in-progress	

AMR - PLANNED COST SCHEDULE

DATE TASK APPROVED BY CO	TASK NO.	DOLLAR AMOUNT APPROVED WITH FEE	TOTAL CUMULATIVE AMOUNT WITH FEE	START DATE	STOP DATE	DURATION
07/02/86	8601	$375,973	$ 375,973	06/02/86	07/31/88	26 months
07/08/86	8602	$ 62,714	$ 438,687	06/18/86	07/31/88	26 months
07/18/86	8603	$180,343	$ 619,030	07/01/86	05/01/87	10 months
08/26/86	8604	$ 88,628	$ 707,658	07/01/86	07/31/88	24 months
10/20/86	8701	$ 59,887	$ 767,545	10/28/86	03/31/87	5 months
11/04/86	8702	$ 18,328	$ 785,873	10/20/86	01/30/87	3 months
12/04/86	8703	$ 28,496	$ 814,369	10/27/86	02/28/87	4 months
12/04/86	8704	$ 21,190	$ 835,559	10/27/86	02/28/87	4 months
02/25/87	8704 (MOD 1)	$ 4,823	$ 840,382	10/27/86 (02/25/87)	04/30/87	2 months
03/26/87	8705	$ 23,638	$ 864,020	02/12/87	04/30/87	3 months
04/07/87	8602 (MOD 2)	$172,711	$1,036,731	02/11/87 (04/07/87)	12/31/87	9 months
05/29/87	8601 (MOD 1)	$ 7,054	$1,043,785	06/02/87	07/01/88	13 months
06/11/87	8603 (MOD 1)	$ 23,812	$1,067,597	07/01/87	09/30/87	3 months

( ) Effective Date of Modification

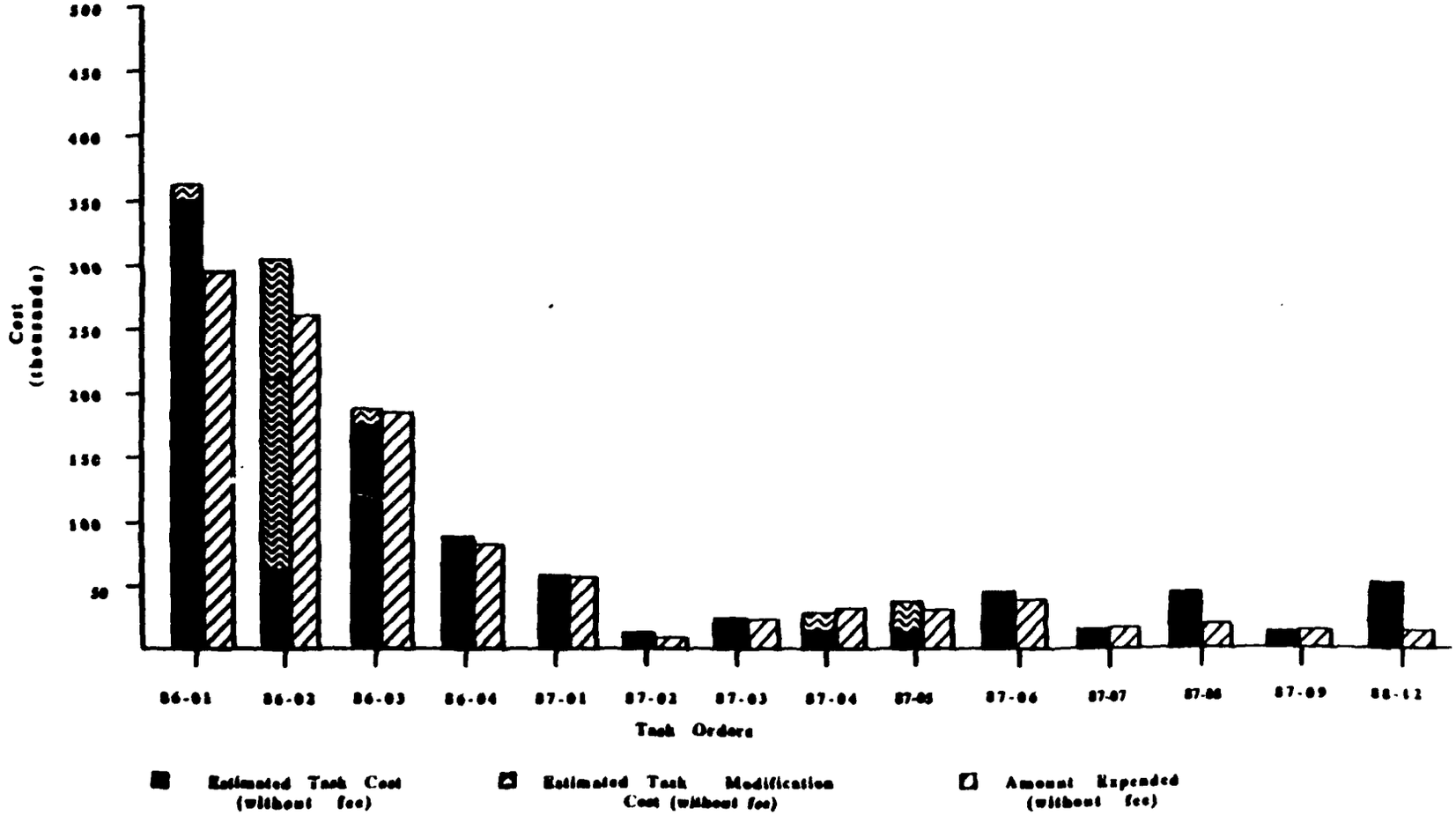
AMR - PLANNED COST SCHEDULE

DATE TASK APPROVED BY CO	TASK NO.	DOLLAR AMOUNT APPROVED WITH FEE	TOTAL CUMULATIVE AMOUNT WITH FEE	START DATE	STOP DATE	DURATION
07/08/87	8705 (MOD 1)	$ 7,069	$1,074,666	07/08/89	09/30/87	3 months
09/21/87	8706	$ 46,125	$1,120,791	08/25/87	12/31/87	4 months
10/07/87	8707	$ 5,467	$1,126,258	09/15/87	11/30/87	3 months
10/23/87	8708	$ 35,567	$1,161,825	09/25/98	12/31/87	3 months
01/22/88	8709	$ 1,260	$1,173,985	11/09/87	02/08/88	3 months
03/03/88	8602 (MOD 4)	$ 60,547	$1,234,532	03/03/88	07/01/88	4 months
04/28/88	8812	$ 35,515	1,270,047	04/20/88	12/30/88	8 months

Estimated vs Expended

Drug Regulatory Affairs Contract

as of 06/24/88



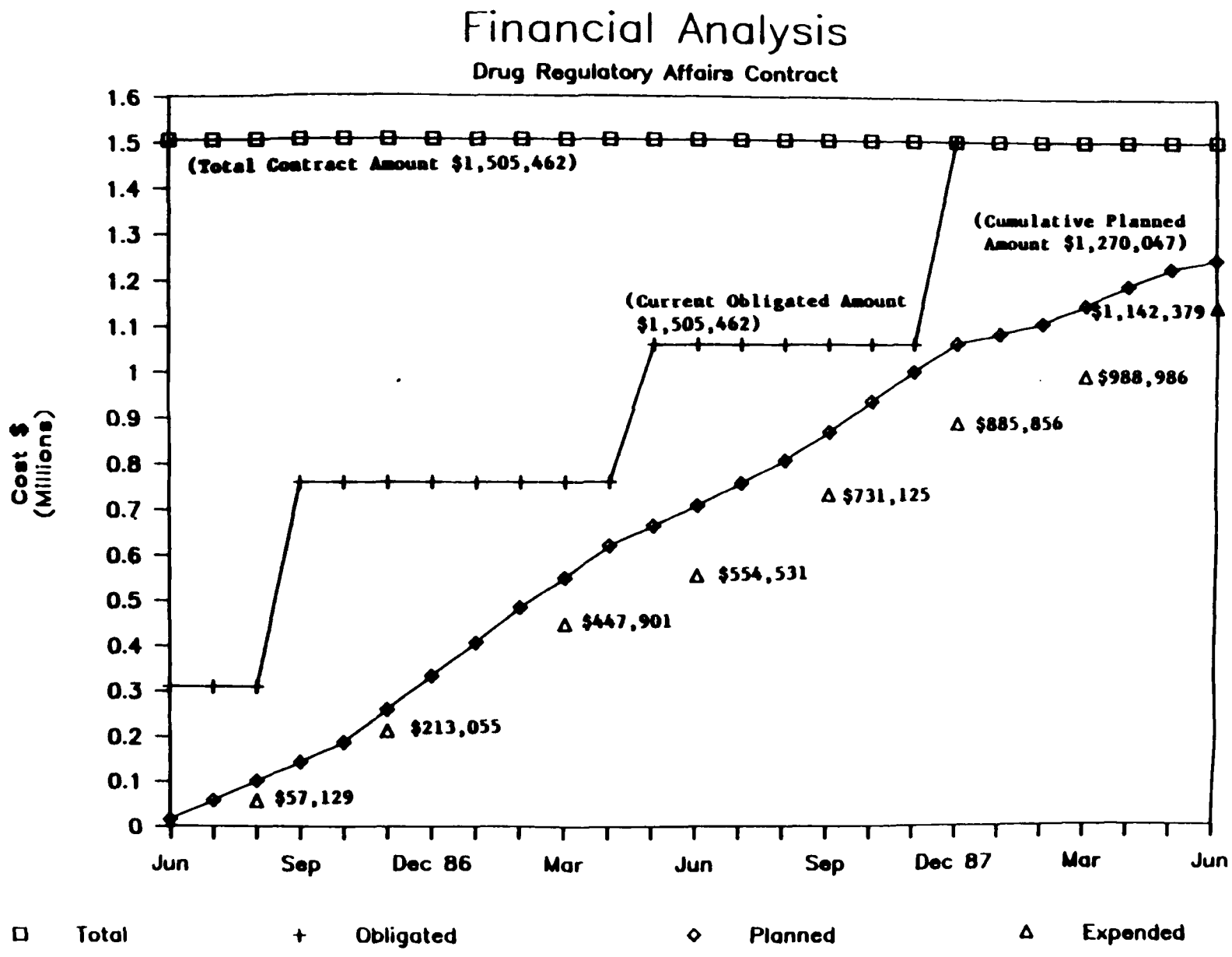
Financial Information[1]
DAMD17-86-C-6189
as of 6/24/88

Task No.	Funds Negotiated	Cost Incurred	$ Expended (%)
8601	$356,636	$293,102	83.6
8602	278,218	255,202	91.7
8603	195,374	186,102[2]	95.2
8604	81,310	81,102	100.5
8701	57,635	55,540	96.4
8702	16,815	15,822	94.1
8703	27,573	27,474[2]	99.6
8704	24,168	24,994	103.4
8705	28,685	28,017	97.7
8706	42,316	41,464[2]	98.0
8707	5,015	5,168	103.1
8708	32,630	26,653	81.7
8709	11,240	11,668	103.8
8811	0	cancelled	0
8812	35,515	10,113	28.5
Total Contract Amount Negotiated	1,488,240		
Amount Expended through 6/24/88		$1,068,053	
Percent of total contract amount negotiated expended through 6/24/88			71.7

(1) These figures do not include fee.

The total number of manhours expended to date is 23,646.

(2) Cost incurred adjusted down to coincide with actual billing to the government - previously over stated for tasks 8603, 8703, 8706.


Financial Analysis
Drug Regulatory Affairs Contract
Cost $ (Millions)
1.6
1.5
1.4
1.3
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
(Total Contract Amount $1,505,462)
(Current Obligated Amount $1,505,462)
(Cumulative Planned Amount $1,270,047)
Δ $57,129
Δ $213,055
Δ $447,901
Δ $554,531
Δ $731,125
Δ $885,856
Δ $988,986
$1,142,379
Jun
Sep
Dec 86
Mar
Jun
Sep
Dec 87
Mar
Jun
Total
Obligated
Planned
Expended

5.0 Summary and Conclusion

Significant progress was made during the first year of the Drug Regulatory Affairs contract. A total of nine tasks and 12 subtasks were submitted to the contractor during the initial performance period. An additional 5 tasks were submitted to the contractor during the second contract year. All tasks/subtasks were completed or are in progress within the projected delivery schedule and cost estimate as described in respective Task Execution Plans. Remaining scheduled work is proceeding on schedule.

This technical progress was achieved through cooperative interaction with the Contracting Officer's Representative, Dr. Carl Nielsen, and other members of the Pharmaceutical Systems Project Management Division. The contractor wishes to express appreciation for the continued excellent and cooperative professional relationship.

6.0 Recommendations

An Annual Program Plan identifying the type of upcoming tasks and projected schedules would be of great value to the contractor and USAMMDA. This plan would facilitate better planning and administration of the task orders under this contract. EER is available to assist or prepare such a plan, if desired.

DISTRIBUTION LIST

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